NMCP COVID-19 Literature Report #82: Friday, 03 December 2021

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Purpose: These reports, published every other week on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers.

All reports are available online at https://nmcp.libguides.com/covidreport. Access is private; you will need to use the direct link or bookmark the URL.

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Please feel free to reach out with questions, suggestions for future topics, or any other feedback.

TABLE OF CONTENTS

Topic . . . . . page; click link to jump to section.

The Big Picture **2**

SARS-CoV-2 Virus and Variants **3**

COVID-19 Vaccines **4**

Breakthrough Infections, Reinfections, and Coinfections **10**

Treatments and Management **14**

Pre-Existing Conditions, Comorbidities, and Impact on Other Health Issues **16**

Long COVID / Post-COVID Period **19**

Pediatric Population **22**

Healthcare Workers **25**

Disparities and Health Equity **28**

Risk, Transmission, and Exposure **29**

Other Infectious Diseases and Public Health Threats **31**

Statistics **32**

References **33**

The Big Picture

News in Brief

Merriam-Webster has declared "vaccine" is the word of the year for 2021 (M-W; image used without permission).

"CEPI to expand COVID-19 vaccine testing network to assess countermeasures to other epidemic threats" (HPN).

"Total COVID deaths in Europe could exceed 2.2 million by March – WHO" (Reuters).

"World Health Assembly agrees to launch process to develop historic global accord on pandemic prevention, preparedness and response" (WHO; see also: Washington Post article).

And Now For Something Completely Different

Supply chain issues along with holiday shopping pressures have caused shortages in many things, including what you might put on your pancakes. But don't worry, our allies to the north have you covered: "Why Canada is unlocking its vault of maple syrup" (CBC).

Journal Articles

JAMA Intern Med: Leading Causes of Death Among Adults Aged 25 to 44 Years by Race and Ethnicity in Texas During the COVID-19 Pandemic, March to December 2020 (22 November 2021)

> "This cohort study examines mortality data from Texas, a racially and ethnically diverse state, to better understand excess mortality among adults aged 25 to 44 years during early months of the COVID-19 pandemic….
>
> Results of this cohort study demonstrated that during March through December 2020, the first 10 months of the COVID-19 pandemic in the US, COVID-19 was the second leading cause of death among Black, Hispanic, and White residents of Texas aged 25 to 44 years, and the most common cause during the third quarter of 2020, with a markedly disproportionate increase in mortality among Hispanic residents."

SARS-CoV-2 Virus and Variants

News in Brief

New Variant: Omicron

A new variant of concern, omicron, has been identified (WHO; CDC).

As of this writing, the omicron variant has been identified in 38 countries, including the US (CNBC). 5 states have reported COVID cases with the omicron variant:

- the first case was documented in California (NPR);
- New York noted 5 cases (Gothamist);
- Minnesota reported a resident with no history of international travel (STAT);
- and there are cases in Colorado and Hawaii caused by the new variant (CNBC).

What to Know About Omicron

"What's known and unknown about Omicron, the coronavirus variant identified in South Africa" (STAT).

"The mystery of where omicron came from — and why it matters" (NPR).

"Some experts suggest Omicron variant may have evolved in an animal host" (STAT).

"Why top virologist is concerned about omicron — Trevor Bedford, PhD, says the new variant 'feels like January 2020 all over again'" (Medpage).

"We'll know more soon about Omicron. Here's how to interpret the coming flood of data" (STAT).

"Omicron's best- and worst-case — a new, highly contagious variant could have terrible consequences. But if it ends up causing milder symptoms than Delta, there's a real upside" (Atlantic).

Transmission and Tracking

"At least 17 suspected Omicron Covid-19 cases after Oslo Christmas party" (AFP).

"U.S. races to detect and track omicron, hampered by an unwieldy surveillance system" (NPR).

"Omicron COVID variant was in Europe before South African scientists detected and flagged it to the world" (CBS; see also: statement from RIVM).

"Omicron-variant border bans ignore the evidence, say scientists" (Nature).

Journal Articles

Survival: The Contested Origin of SARS-CoV-2 (26 November 2021)

> "This article describes what is known about the origin of SARS-CoV-2, with implications for policy, biological research and public-health surveillance. Theories about the origin include a natural emergence; a laboratory accident with a naturally harvested strain; an accident with a naturally harvested strain modified in a laboratory; and the deliberate creation of a biological weapon. While available scientific evidence points to a natural zoonotic event as the origin of SARS-CoV-2, this paper recommends specific steps governments and scientific institutions should take to address uncertainties about the origin of the COVID-19 pandemic, as well as to make all potential causes for a pandemic less likely to produce one in the future. Immediate steps include promoting international scientific collaboration, addressing scientific misinformation and disinformation, fully implementing 'One Health' and reining in the illegal wildlife trade."

COVID-19 Vaccines

News in Brief

"What J&J can still teach us — a vaccine's value isn't just in its peak performance" (Atlantic).

"What the Moderna–NIH COVID vaccine patent fight means for research" (Nature).

"Why Puerto Rico is a leader in vaccinating against COVID-19" (NPR).

Boosters

"CDC expands COVID-19 booster recommendations" (CDC).

"Pfizer set to request authorization for coronavirus booster for 16- and 17-year-olds" (WP).

"Omicron is supercharging the COVID vaccine booster debate" (Nature).

Adverse Events / Side Effects

"Scientists find clues to what triggers rare blood clots in AstraZeneca coronavirus vaccine" (WP; see also: Sci Adv paper).

Vaccine Development

"A different kind of COVID vaccine is about ready to roll" (NPR).

"Moderna says an omicron variant vaccine could be ready in early 2022" (CNBC).

DYI, Vaccine Edition

"Frustrated by vaccine inequity, a South African lab rushes to replicate Moderna's shot" (WP).

"Cuba's bet on home-grown COVID vaccines is paying off" (Nature).

Just… maybe don't make your own vaccine whole cloth, okay? "German doctor faces charges after administering thousands of self-made vaccines" (Irish Times).

Special Reports and Other Resources

JHCHS: A Waypoint on the Path to Health Equity: COVID-19 Vaccination at Month 11 (23 November 2021)

> "This CommuniVax Coalition report represents a waypoint in the COVID-19 pandemic: an opportunity to pause to mark the distance traveled, alter the course if necessary, and set out on the next part of the journey. It describes progress made toward greater equity in the COVID-19 vaccination campaign and proposes steps to advance even further. CommuniVax is a national rapid research coalition of social scientists, public health experts, healthcare providers, and community advocates, and a part of the larger community of practice that has observed and participated in the COVID-19 vaccine rollout through an equity lens.
>
> Earlier in the year, it was estimated that COVID-19 vaccines had averted nearly 140,000 deaths and between $625 billion and $1.4 trillion in associated costs in the United States. Initially, however, these enormous, lifesaving benefits were not equitably distributed to communities of Black, Indigenous, and other people of color (BIPOC). Despite early setbacks, more recent progress has been made in reversing inequities in COVID-19 vaccine coverage. In mid- September, similar shares of Hispanic/Latino (73%), African American/Black (70%), and White (71%) adults reported having received at least 1 dose of an approved COVID-19 vaccine.
>
> However, while vaccine coverage is similar across racial/ethnic groups nationally, the same is not true at state and local levels. A better understanding of factors that have facilitated higher vaccine coverage within BIPOC communities in certain parts of the country can aid states and local jurisdictions still struggling with vaccination equity and/or unequal health outcomes. Such an inquiry can also help inform the development of outreach and engagement approaches for White communities that currently account for the largest proportion of unvaccinated individuals in the country.
>
> To contribute to this effort, in early October 2021, CommuniVax undertook an assessment of its work, inviting other similarly engaged groups to reflect on the coalition's efforts and, more generally, on the COVID-19 vaccination rollout. Using a combination of listening sessions and a survey, we gathered feedback from an array of advocates, organizers,

> practitioners, and leaders representing state and local government, the public health sector, academia, professional associations, community-based organizations (CBOs), faith-based organizations (FBOs) and coalitions across the country to document successes, failures, and lessons learned that could be used to shape future efforts of vaccine promotion and health equity strengthening.
>
> From this assessment, we identified early equity “wins” in the COVID-19 vaccine rollout and developed recommendations on how to ensure ongoing advances in health equity, now and into the future."

Journal Articles

Clin Infect Dis: A Higher Antibody Response Is Generated With a 6- to 7-Week (vs Standard) Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Vaccine Dosing Interval (30 November 2021)

> "The optimal dosing interval for severe acute respiratory syndrome coronavirus 2 vaccines remains controversial. In this prospective study, we compared serology results of paramedics vaccinated with mRNA vaccines at the recommended short (17–28 days) vs long (42–49 days) interval. We found that a long dosing interval resulted in higher spike, receptor binding domain, and spike N terminal domain antibody concentrations."

JAMA: Association Between mRNA Vaccination and COVID-19 Hospitalization and Disease Severity (04 November 2021)

> "Question: Does prior COVID-19 vaccination reduce hospitalizations for COVID-19, and among patients hospitalized for COVID-19, does prior vaccination reduce disease severity?
>
> Findings: In a case-control study that included 4513 hospitalized adults in 18 US states, hospitalization for a COVID-19 diagnosis compared with an alternative diagnosis was associated with an adjusted odds ratio (aOR) of 0.15 for full vaccination with an authorized or approved mRNA COVID-19 vaccine. Among adults hospitalized for COVID-19, progression to death or invasive mechanical ventilation was associated with an aOR of 0.33 for full vaccination; both ORs were statistically significant.
>
> Meaning: Vaccination with an mRNA COVID-19 vaccine was significantly less likely among patients with COVID-19 hospitalization and with disease progression, consistent with risk reduction among vaccine breakthrough infections."

Effectiveness

NEJM: Comparative Effectiveness of BNT162b2 and mRNA-1273 Vaccines in U.S. Veterans (01 December 2021)

> "BACKGROUND The messenger RNA (mRNA)–based vaccines BNT162b2 and mRNA-1273 are more than 90% effective against coronavirus disease 2019 (Covid-19). However, their comparative effectiveness for a range of outcomes across diverse populations is unknown.
>
> METHODS We emulated a target trial using the electronic health records of U.S. veterans who received a first dose of the BNT162b2 or mRNA-1273 vaccine between January 4 and May 14, 2021, during a period marked by predominance of the SARS-CoV-2 B.1.1.7 (alpha) variant. We matched recipients of each vaccine in a 1:1 ratio according to their risk factors. Outcomes included documented severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, symptomatic Covid-19, hospitalization for Covid-19, admission to an intensive care unit (ICU) for Covid-19, and death from Covid-19. We estimated risks using the Kaplan–Meier estimator. To assess the influence of the B.1.617.2 (delta) variant, we emulated a second target trial that involved veterans vaccinated between July 1 and September 20, 2021.
>
> RESULTS Each vaccine group included 219,842 persons. Over 24 weeks of follow-up in a period marked by alpha-variant predominance, the estimated risk of documented infection was 5.75 events per 1000 persons (95% confidence interval [CI], 5.39 to 6.23) in the BNT162b2 group and 4.52 events per 1000 persons (95% CI, 4.17 to 4.84) in the mRNA-1273 group. The excess number of events per 1000 persons for BNT162b2 as compared with mRNA-1273 was 1.23 (95% CI, 0.72 to 1.81) for documented infection, 0.44 (95% CI, 0.25 to 0.70) for symptomatic Covid-19, 0.55 (95% CI, 0.36 to 0.83) for hospitalization for Covid-19, 0.10 (95% CI, 0.00 to 0.26) for ICU admission for Covid-19, and 0.02 (95% CI, −0.06 to 0.12) for death from Covid-19. The corresponding excess risk (BNT162b2 vs. mRNA-1273) of documented infection over 12 weeks of follow-up in a period marked by delta-variant predominance was 6.54 events per 1000 persons (95% CI, −2.58 to 11.82).
>
> CONCLUSIONS The 24-week risk of Covid-19 outcomes was low after vaccination with mRNA-1273 or BNT162b2, although risks were lower with mRNA-1273 than with BNT162b2. This pattern was consistent across periods marked by alpha- and delta-variant predominance."

NEJM: Covid-19 Vaccine Effectiveness in New York State (01 December 2021)

> "BACKGROUND Population-based data from the United States on the effectiveness of the three coronavirus disease 2019 (Covid-19) vaccines currently authorized by the Food and Drug Administration are limited. Whether declines in effectiveness are due to waning

> immunity, the B.1.617.2 (delta) variant of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), or other causes is unknown.
>
> METHODS We used data for 8,690,825 adults in New York State to assess the effectiveness of the BNT162b2, mRNA-1273, and Ad26.COV2.S vaccines against laboratory-confirmed Covid-19 and hospitalization with Covid-19 (i.e., Covid-19 diagnosed at or after admission). We compared cohorts defined according to vaccine product received, age, and month of full vaccination with age-specific unvaccinated cohorts by linking statewide testing, hospital, and vaccine registry databases. We assessed vaccine effectiveness against Covid-19 from May 1 through September 3, 2021, and against hospitalization with Covid-19 from May 1 through August 31, 2021.
>
> RESULTS There were 150,865 cases of Covid-19 and 14,477 hospitalizations with Covid-19. During the week of May 1, 2021, when the delta variant made up 1.8% of the circulating variants, the median vaccine effectiveness against Covid-19 was 91.3% (range, 84.1 to 97.0) for BNT162b2, 96.9% (range, 93.7 to 98.0) for mRNA-1273, and 86.6% (range, 77.8 to 89.7) for Ad26.COV2.S. Subsequently, effectiveness declined contemporaneously in all cohorts, from a median of 93.4% (range, 77.8 to 98.0) during the week of May 1 to a nadir of 73.5% (range, 13.8 to 90.0) around July 10, when the prevalence of the delta variant was 85.3%. By the week of August 28, when the prevalence of the delta variant was 99.6%, the effectiveness was 74.2% (range, 63.4 to 86.8). Effectiveness against hospitalization with Covid-19 among adults 18 to 64 years of age remained almost exclusively greater than 86%, with no apparent time trend. Effectiveness declined from May through August among persons 65 years of age or older who had received BNT162b2 (from 94.8 to 88.6%) or mRNA-1273 (from 97.1 to 93.7%). The effectiveness of Ad26.COV2.S was lower than that of the other vaccines, with no trend observed over time (range, 80.0 to 90.6%).
>
> CONCLUSIONS The effectiveness of the three vaccines against Covid-19 declined after the delta variant became predominant. The effectiveness against hospitalization remained high, with modest declines limited to BNT162b2 and mRNA-1273 recipients 65 years of age or older."

Clin Infect Dis: BNT162b2 mRNA Vaccine Effectiveness Given Confirmed Exposure: Analysis of Household Members of COVID-19 Patients (24 November 2021)

> "Background: While BNT162b2 vaccine-efficacy analyses were previously published, the effectiveness of the vaccine in preventing COVID-19 given confirmed exposure has not been previously demonstrated, even though it has policy implications, such as the need for self-quarantine when exposure has occurred or protective measures for vaccinated individuals in high-risk areas.
>
> Methods: In a retrospective cohort study, we used data collected between 20/12/2020 and 17/03/2021 from the second largest healthcare provider in Israel to analyze the probability

> of an additional household infection occurring within 10 days after an index infection. In model 1, vaccine effectiveness was described for Fully Vaccinated individuals (7 or more days from second dose) versus either Unvaccinated participants or those Recently Vaccinated Once (0-7 days from the first dose, presumably still unprotected). Secondary analyses included correction for differing testing rates. In model 2, we conducted a separate analysis of households comprised of only adults with the same vaccination status.
>
> Results: 173,569 households were included, of which 6,351 households had an index infection (mean [SD] age, 58.9 [13.5] years; 50% were women).Adjusted vaccine effectiveness of Fully Vaccinated compared to Unvaccinated participants was 80.3% [95% CI, 73.5 to 85.4] and 82.0% [95% CI, 75.6 to 86.8] compared to those Recently Vaccinated Once.
>
> Conclusions: The BNT162b2 vaccine is effective in a high-risk real-life exposure scenario, but the protection rates afforded in these settings are lower than those previously described. Household members of patients infected with SARS-CoV-2 and individuals with a confirmed significant exposure to SARS-CoV-2 are still at risk of being infected even if fully vaccinated."

Adverse Events / Side Effects

Emerg Infect Dis: Postvaccination multisystem inflammatory syndrome in adult with no evidence of prior SARS-CoV-2 infection (01 December 2021)

> "Ten days after receiving the first dose of coronavirus disease vaccine, a 22-year-old woman in South Korea experienced myocarditis, myopathy, pericarditis, and gastroenteritis; rash subsequently developed. There was no evidence of prior infection with severe acute respiratory syndrome coronavirus 2. The diagnosis was multisystem inflammatory syndrome resulting from coronavirus disease vaccination."

Clin Infect Dis: Multisystem Inflammatory Syndrome in Adults after SARS-CoV-2 infection and COVID-19 vaccination (28 November 2021)

> "Background: Multisystem inflammatory syndrome in adults (MIS-A) was reported in association with the COVID-19 pandemic. MIS-A was included in the list of adverse events to be monitored as part of the emergency use authorizations issued for COVID-19 vaccines.
>
> Methods: Reports of MIS-A patients received by the Centers for Disease Control and Prevention (CDC) after COVID-19 vaccines became available were assessed. Data collected on the patients included clinical and demographic characteristics and their vaccine status. The Vaccine Adverse Events Reporting System (VAERS) was also reviewed for possible cases of MIS-A.
>
> Results: From December 14, 2020 to April 30, 2021, 20 patients who met the case definition for MIS-A were reported to CDC. Their median age was 35 years (range, 21-66 years), and

> 13 (65%) were male. Overall, 16 (80%) patients had a preceding COVID-19-like illness a median of 26 days (range 11-78 days) before MIS-A onset. All 20 patients had laboratory evidence of SARS-CoV-2 infection. Seven MIS-A patients (35%) received COVID-19 vaccine a median of 10 days (range, 6-45 days) before MIS-A onset; 3 patients received a second dose of COVID-19 vaccine 4, 17, and 22 days before MIS-A onset. Patients with MIS-A predominantly had gastrointestinal and cardiac manifestations and hypotension or shock.
>
> Conclusions: Although 7 patients were reported to have received COVID-19 vaccine, all had evidence of prior SARS-CoV-2 infection. Given the widespread use of COVID-19 vaccines, the lack of reporting of MIS-A associated with vaccination alone, without evidence of underlying SARS-CoV-2 infection, is reassuring."

JAMA: Myocardial Infarction, Stroke, and Pulmonary Embolism After BNT162b2 mRNA COVID-19 Vaccine in People Aged 75 Years or Older (22 November 2021)

> "This population based study evaluated the short-term risk of severe cardiovascular risks among French residents 75 years or older after they received the BNT162b2 mRNA vaccination….
>
> In this nationwide study involving persons aged 75 years or older in France, no increase in the incidence of acute myocardial infarction, stroke, and pulmonary embolism was detected 14 days following each BNT162b2 mRNA vaccine dose.
>
> Israeli and US studies reported that persons receiving the BNT162b2 vaccine were not at increased risk of myocardial infarction, pulmonary embolism, or cerebrovascular events in the 42 days and 21 days following vaccination. Based on a self-controlled case-series design that compensates for the lack of randomization by eliminating the effect of time-invariant confounding factors, this study provides further evidence regarding the risk of serious cardiovascular adverse events in older people."

Breakthrough Infections, Reinfections, and Coinfections

News in Brief

"South Africa is seeing an increase in COVID-19 reinfections due to the Omicron variant but symptoms for reinfected patients and those infected after vaccination appear to be mild, a scientist studying the outbreak of the new strain said" (Reuters; see also: medRxiv preprint [not yet peer reviewed] and Twitter thread from lead author).

"COVID hit 13 members of their family the first time. A year later it struck again" (NPR).

Journal Articles

JAMA Intern Med: Odds of Testing Positive for SARS-CoV-2 Following Receipt of 3 vs 2 Doses of the BNT162b2 mRNA Vaccine (30 November 2021)

> "Question: What is the additional reduction in the odds of infection with SARS-CoV-2 in people receiving a third dose (booster) of the BNT162b2 (Pfizer-BioNTech) vaccine compared with those receiving 2 doses?
>
> Findings: In this case-control study that included 306 710 Israeli adults 40 years and older, there was an estimated significant reduction in the odds of SARS-CoV-2 infection within a few weeks of receiving the booster compared with receiving just the 2 primary doses. Those receiving the booster also had lower odds of hospitalization.
>
> Meaning: The findings of this study suggest that the waning of vaccine-induced protection against SARS-CoV-2 infection seems to be counteracted in the short-term by a third dose and further monitoring is needed to determine the duration of immunity following the booster."

J Med Econ: Evaluation of COVID-19 vaccine breakthrough infections among immunocompromised patients fully vaccinated with BNT162b2 (30 November 2021)

> "Objective: To evaluate COVID-19 vaccine breakthrough infections among immunocompromised (IC) individuals.
>
> Methods: Individuals vaccinated with BNT162b2 were selected from the US HealthVerity database (10 December 2020 to 8 July 2021). COVID-19 vaccine breakthrough infections were examined in fully vaccinated (≥14 days after 2nd dose) IC individuals (IC cohort), 12 mutually exclusive IC condition groups, and a non-IC cohort. IC conditions were identified using an algorithm based on diagnosis codes and immunosuppressive (IS) medication usage.
>
> Results: Of 1,277,747 individuals ≥16 years of age who received 2 BNT162b2 doses, 225,796 (17.7%) were identified as IC (median age: 58 years; 56.3% female). The most prevalent IC conditions were solid malignancy (32.0%), kidney disease (19.5%), and rheumatologic/inflammatory conditions (16.7%). Among the fully vaccinated IC and non-IC cohorts, a total of 978 breakthrough infections were observed during the study period; 124 (12.7%) resulted in hospitalization and 2 (0.2%) were inpatient deaths. IC individuals accounted for 38.2% (N = 374) of all breakthrough infections, 59.7% (N = 74) of all hospitalizations, and 100% (N = 2) of inpatient deaths. The proportion with breakthrough infections was 3 times higher in the IC cohort compared to the non-IC cohort (N = 374 [0.18%] vs. N = 604 [0.06%]; unadjusted incidence rates were 0.89 and 0.34 per 100 person-years, respectively. Organ transplant recipients had the highest incidence rate; those with >1 IC condition, antimetabolite usage, primary immunodeficiencies, and hematologic malignancies also had higher incidence rates compared to the overall IC cohort. Incidence

> rates in older (≥65 years old) IC individuals were generally higher versus younger IC individuals (<65).
>
> Limitations: This retrospective analysis relied on coding accuracy and had limited capture of COVID-19 vaccine receipt.
>
> Conclusions: COVID-19 vaccine breakthrough infections are rare but are more common and severe in IC individuals. The findings from this large study support the FDA authorization and CDC recommendations to offer a 3rd vaccine dose to increase protection among IC individuals."

Emerg Infect Dis: Systematic genomic and clinical analysis of severe acute respiratory syndrome coronavirus 2 reinfections and recurrences involving the same strain (29 November 2021)

> "Estimates of the burden of severe acute respiratory syndrome coronavirus 2 reinfections are limited by the scarcity of population-level studies incorporating genomic support. We conducted a systematic study of reinfections in Madrid, Spain, supported by genomic viral analysis and host genetic analysis, to cleanse laboratory errors and to discriminate between reinfections and recurrences involving the same strain. Among the 41,195 cases diagnosed (March 2020–March 2021), 93 (0.23%) had 2 positive reverse transcription PCR tests (55–346 days apart). After eliminating cases with specimens not stored, of suboptimal sequence quality, or belonging to different persons, we obtained valid data from 22 cases. Of those, 4 (0.01%) cases were recurrences involving the same strain; case-patients were 39–93 years of age, and 3 were immunosuppressed. Eighteen (0.04%) cases were reinfections; patients were 19–84 years of age, and most had no relevant clinical history. The second episode was more severe in 8 cases."

NEJM: Severity of SARS-CoV-2 Reinfections as Compared with Primary Infections (24 November 2021)

> "A team led by Weill Cornell Medicine-Qatar researchers compared primary COVID-19 cases from March through June 2020 with reinfections from January through April 2021, a wave fueled by the Alpha (B117) and Beta (B1351) variants but before the emergence of Delta (B1617.2). After the first pandemic wave, 40% of the population had measurable antibodies against the coronavirus.
>
> The team used data on 353,326 Qataris with primary infection or reinfection to investigate the risk of severe disease leading to hospitalization, critical disease leading to admission to an intensive care unit, and fatal disease.
>
> Among 1,304 reinfections, 31.7% were caused by the Beta variant, 4.4% were Alpha cases, 16.3% were wild-type infections, and 47.6% had unknown origins. Median time between primary infection and reinfection was 277 days.

> Reinfections were rare and generally mild, perhaps because the immune system had already been primed. The chances of severe disease at reinfection were much lower than at primary infection (odds ratio [OR], 0.12).
>
> No reinfections caused critical disease, compared with 28 at primary infection (OR, 0.00). No reinfected patients died, versus 7 with primary infections (OR, 0.00). The chances of the composite outcome of severe, critical, or fatal disease among reinfected patients were also much lower than at primary infection (OR, 0.10).
>
> Reinfected patients had 90% lower odds of hospitalization or death than those at primary infection. Four reinfections were severe enough to lead to hospitalization, but all ended in recovery.
>
> The authors said future research should determine whether natural immunity against severe illness at reinfection protects longer, similar to how short-term immunity develops against seasonal coronaviruses such as those that cause the common cold, with longer-lasting immunity against severe disease at reinfection.
>
> "If this were the case with SARS-CoV-2, the virus (or at least the variants studied to date) could adopt a more benign pattern of infection when it becomes endemic," the researchers concluded." (summary from: CIDRAP)

Emerg Infect Dis: Multistate Outbreak of SARS-CoV-2 Infections, Including Vaccine Breakthrough Infections, Associated with Large Public Gatherings, United States (18 November 2021)

> "During July 2021, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) B.1.617.2 variant infections, including vaccine breakthrough infections, occurred after large public gatherings in Provincetown, Massachusetts, USA, prompting a multistate investigation. Public health departments identified primary and secondary cases by using coronavirus disease surveillance data, case investigations, and contact tracing. A primary case was defined as SARS-CoV-2 detected <14 days after travel to or residence in Provincetown during July 3–17. A secondary case was defined as SARS-CoV-2 detected <14 days after close contact with a person who had a primary case but without travel to or residence in Provincetown during July 3–August 10. We identified 1,098 primary cases and 30 secondary cases associated with 26 primary cases among fully and non–fully vaccinated persons. Large gatherings can have widespread effects on SARS-CoV-2 transmission, and fully vaccinated persons should take precautions, such as masking, to prevent SARS-CoV-2 transmission, particularly during substantial or high transmission."

Treatments and Management

News in Brief

"FDA advisers narrowly recommend authorization of first antiviral pill to treat covid-19" (WP).

"How Pfizer developed a COVID pill in record time" (NPR).

"Covid antivirals could be pandemic game-changers. But Americans might struggle to access them" (STAT).

"The new COVID drugs are a bigger deal than people realize — vaccines are amazing, but people who become infected need effective treatments" (Atlantic).

"Once rare, lung transplants for COVID-19 patients are rising quickly" (NPR).

Journal Articles

Lancet Respir Med: Lenzilumab in hospitalised patients with COVID-19 pneumonia (LIVE-AIR): a phase 3, randomised, placebo-controlled trial (01 December 2021)

> "Background: The pathophysiology of COVID-19 includes immune-mediated hyperinflammation, which could potentially lead to respiratory failure and death. Granulocyte-macrophage colony-stimulating factor (GM-CSF) is among cytokines that contribute to the inflammatory processes. Lenzilumab, a GM-CSF neutralising monoclonal antibody, was investigated in the LIVE-AIR trial to assess its efficacy and safety in treating COVID-19 beyond available treatments.
>
> Methods: In LIVE-AIR, a phase 3, randomised, double-blind, placebo-controlled trial, hospitalised adult patients with COVID-19 pneumonia not requiring invasive mechanical ventilation were recruited from 29 sites in the USA and Brazil and were randomly assigned (1:1) to receive three intravenous doses of lenzilumab (600 mg per dose) or placebo delivered 8 h apart. All patients received standard supportive care, including the use of remdesivir and corticosteroids. Patients were stratified at randomisation by age and disease severity. The primary endpoint was survival without invasive mechanical ventilation to day 28 in the modified intention-to-treat population (mITT), comprising all randomised participants who received at least one dose of study drug under the documented supervision of the principal investigator or sub-investigator. Adverse events were assessed in all patients who received at least one dose of study drug. This trial is registered with ClinicalTrials.gov, NCT04351152, and is completed.
>
> Findings: Patients were enrolled from May 5, 2020, until Jan 27, 2021. 528 patients were screened, of whom 520 were randomly assigned and included in the intention-to-treat population. 479 of these patients (n=236, lenzilumab; n=243, placebo) were included in the

> mITT analysis for the primary outcome. Baseline demographics were similar between groups. 311 (65%) participants were males, mean age was 61 (SD 14) years at baseline, and median C-reactive protein concentration was 79 (IQR 41–137) mg/L. Steroids were administered to 449 (94%) patients and remdesivir to 347 (72%) patients; 331 (69%) patients received both treatments. Survival without invasive mechanical ventilation to day 28 was achieved in 198 (84%; 95% CI 79–89) participants in the lenzilumab group and in 190 (78%; 72–83) patients in the placebo group, and the likelihood of survival was greater with lenzilumab than placebo (hazard ratio 1·54; 95% CI 1·02–2·32; p=0·040). 68 (27%) of 255 patients in the lenzilumab group and 84 (33%) of 257 patients in the placebo group experienced at least one adverse event that was at least grade 3 in severity based on CTCAE criteria. The most common treatment-emergent adverse events of grade 3 or higher were related to respiratory disorders (26%) and cardiac disorders (6%) and none led to death.
>
> Interpretation: Lenzilumab significantly improved survival without invasive mechanical ventilation in hospitalised patients with COVID-19, with a safety profile similar to that of placebo. The added value of lenzilumab beyond other immunomodulators used to treat COVID-19 alongside steroids remains unknown."

JAMA Netw Open: Effect of High-Titer Convalescent Plasma on Progression to Severe Respiratory Failure or Death in Hospitalized Patients With COVID-19 Pneumonia: A Randomized Clinical Trial (29 November 2021)

> "Question: Is convalescent plasma useful in preventing worsening respiratory failure or death in patients with COVID-19 pneumonia?
>
> Findings: In this randomized clinical trial of 487 patients with COVID-19 pneumonia and a partial pressure of arterial oxygen–to–fraction of inspired oxygen (Pao2/Fio2) ratio between 350 and 200 mm Hg at enrollment, the rate of the primary clinical end point (need for mechanical ventilation, defined as Pao2/Fio2 ratio <150 mm Hg, or death) was not significantly different between the convalescent plasma group and the control group.
>
> Meaning: In this trial, convalescent plasma did not reduce the progression to severe respiratory failure or death within 30 days."

JAMA Intern Med: Efficacy of Inhaled Ciclesonide for Outpatient Treatment of Adolescents and Adults With Symptomatic COVID-19: A Randomized Clinical Trial (22 November 2021)

> "Question: Can the inhaled steroid ciclesonide reduce the time to alleviation of all COVID-19–related symptoms among nonhospitalized participants with symptomatic COVID-19 infection?
>
> Findings: In this randomized clinical trial of 400 patients with symptomatic COVID-19, ciclesonide did not reduce the time to alleviation of all COVID-19–related symptoms.

> However, patients who were treated with ciclesonide had fewer subsequent emergency department visits or hospital admissions for reasons that were related to COVID-19.
>
> Meaning: The results of this randomized clinical trial suggest that future studies of inhaled steroids are needed to explore their efficacy in patients with a high risk for disease progression and in reducing the incidence of long-term COVID-19 symptoms or postacute sequelae of SARS-CoV-2."

Pre-Existing Conditions, Comorbidities, and Impact on Other Health Issues

News in Brief

"Cancer patients hope infusions might enhance protection against Covid" (STAT).

Journal Articles

JAMA Netw Open: Rituximab Infusion Timing, Cumulative Dose, and Hospitalization for COVID-19 in Persons With Multiple Sclerosis in Sweden (01 December 2021)

> "This case-control study examines the risk of severe COVID-19 infection in individuals with multiple sclerosis who were receiving rituximab….
>
> Among 172 Swedish persons with multiple sclerosis who received rituximab before contracting COVID-19, we found no statistically significant association between the timing of rituximab infusion or cumulative lifetime rituximab dose and the odds of hospitalization for COVID-19, although the study power was limited."

PLoS Med: Prevalence and determinants of healthcare avoidance during the COVID-19 pandemic: A population-based cross-sectional study (23 November 2021)

> "Background: During the Coronavirus Disease 2019 (COVID-19) pandemic, the number of consultations and diagnoses in primary care and referrals to specialist care declined substantially compared to prepandemic levels. Beyond deferral of elective non-COVID-19 care by healthcare providers, it is unclear to what extent healthcare avoidance by community-dwelling individuals contributed to this decline in routine healthcare utilisation. Moreover, it is uncertain which specific symptoms were left unheeded by patients and which determinants predispose to healthcare avoidance in the general population. In this cross-sectional study, we assessed prevalence of healthcare avoidance during the pandemic from a patient perspective, including symptoms that were left unheeded, as well as determinants of healthcare avoidance.

> Methods and findings: On April 20, 2020, a paper COVID-19 survey addressing healthcare utilisation, socioeconomic factors, mental and physical health, medication use, and COVID-19-specific symptoms was sent out to 8,732 participants from the population-based Rotterdam Study (response rate 73%). All questionnaires were returned before July 10, 2020. By hand, prevalence of healthcare avoidance was subsequently verified through free text analysis of medical records of general practitioners. Odds ratios (ORs) for avoidance were determined using logistic regression models, adjusted for age, sex, and history of chronic diseases. We found that 1,142 of 5,656 included participants (20.2%) reported having avoided healthcare. Of those, 414 participants (36.3%) reported symptoms that potentially warranted urgent evaluation, including limb weakness (13.6%), palpitations (10.8%), and chest pain (10.2%). Determinants related to avoidance were older age (adjusted OR 1.14 [95% confidence interval (CI) 1.08 to 1.21]), female sex (1.58 [1.38 to 1.82]), low educational level (primary education versus higher vocational/university 1.21 [1.01 to 1.46), poor self-appreciated health (per level decrease 2.00 [1.80 to 2.22]), unemployment (versus employed 2.29 [1.54 to 3.39]), smoking (1.34 [1.08 to 1.65]), concern about contracting COVID-19 (per level increase 1.28 [1.19 to 1.38]) and symptoms of depression (per point increase 1.13 [1.11 to 1.14]) and anxiety (per point increase 1.16 [1.14 to 1.18]). Study limitations included uncertainty about (perceived) severity of the reported symptoms and potentially limited generalisability given the ethnically homogeneous study population.
>
> Conclusions: In this population-based cross-sectional study, 1 in 5 individuals avoided healthcare during lockdown in the COVID-19 pandemic, often for potentially urgent symptoms. Healthcare avoidance was strongly associated with female sex, fragile self-appreciated health, and high levels of depression and anxiety. These results emphasise the need for targeted public education urging these vulnerable patients to timely seek medical care for their symptoms to mitigate major health consequences."

JAMA Netw Open: Factors Associated With Risk of Postdischarge Thrombosis in Patients With COVID-19 (22 November 2021)

> "Question: Which patients with COVID-19 may benefit from extended thromboprophylaxis following hospital discharge?
>
> Findings: In this cohort study of 2832 patients hospitalized with COVID-19, postdischarge venous thromboembolic events occurred more often in those with a history of venous thromboembolism, peak dimerized plasmin fragment D (D-dimer) level greater than 3 µg/mL, and predischarge C-reactive protein level greater than 10 mg/dL. Patients who received postdischarge anticoagulation therapy had fewer events.
>
> Meaning: These findings suggest that postdischarge anticoagulation therapy may be considered for high-risk patients with COVID-19."

Cancer Patients

JAMA Oncol: Association of COVID-19 Vaccination With SARS-CoV-2 Infection in Patients With Cancer: A US Nationwide Veterans Affairs Study (02 December 2021)

> "Question: What is the effectiveness of SARS-CoV-2 vaccination in patients with cancer?
>
> Findings: In this cohort study of US Veterans Affairs patients who received systemic therapy for cancer between August 15, 2010, and May 4, 2021, a proxy measure for effectiveness of the vaccine starting 14 days after the second dose was 58%. The measure of effectiveness starting 14 days after the second dose was 85% in patients who had not received systemic therapy within the 6 months prior to vaccination and 76% among those receiving hormonal treatment.
>
> Meaning: Results suggest that SARS-CoV-2 vaccination associated with lower infection rates in patients with cancer, especially in those not receiving current systemic therapy and those receiving hormonal treatment."

JAMA Oncol: Time-Dependent COVID-19 Mortality in Patients With Cancer: An Updated Analysis of the OnCovid Registry (24 November 2021)

> "Question: Has COVID-19 mortality in patients with cancer improved during the course of the pandemic in Europe?
>
> Findings: In this registry-based study of 2634 patients in 6 European countries with COVID-19 and cancer, there was significant time-dependent improvement in the risk of death at 14 days and at 3 months.
>
> Meaning: Mortality from COVID-19 has improved; this improvement may be associated with earlier diagnosis and improved disease management."

JAMA Oncol: Assessment of Response to a Third Dose of the SARS-CoV-2 BNT162b2 mRNA Vaccine in Patients With Solid Tumors Undergoing Active Treatment (23 November 2021)

> "This cohort study evaluates the short-term humoral response to a third dose of the SARS-CoV-2 BNT162b2 vaccine in patients undergoing acute systemic therapy for solid tumors….
>
> Although limited by a small sample size, data in this cohort study suggest a generally positive and immediate antibody response to booster administration of the BNT162b2 vaccine among patients with cancer receiving active systemic therapy. These results align with other recent findings showing swift, substantial response in comparable booster-dosed populations (eg, solid organ transplant recipients). As for clinical ramifications, the present results support booster dosing of patients with cancer, including individuals being treated with chemotherapy."

JAMA Oncol: Assessment of 4 Doses of SARS-CoV-2 Messenger RNA-Based Vaccine in Recipients of a Solid Organ Transplant (24 November 2021)

> "This case series study assesses whether a fourth dose of a SARS-CoV-2 messenger RNA (mRNA)–based vaccine is associated with improved anti–SARS-CoV-2 antibody response in solid organ transplant recipients in France."

Long COVID / Post-COVID Period

News in Brief

"Do vaccines protect against long COVID? What the data say" (Nature).

"For patients with long COVID, chronic fatigue syndrome may offer a guiding star" (NPR).

Long read: "Even health-care workers with long COVID are being dismissed — Medical professionals are used to being believed, but as patients, they found that their expertise didn't matter" (Atlantic).

Listen: "Living with Long COVID" (NPR).

Journal Articles

Front Med: COVID-19 Post-acute Sequelae Among Adults: 12 Month Mortality Risk (01 December 2021)

> "Background: There are concerns regarding post-acute sequelae of COVID-19, but it is unclear whether COVID-19 poses a significant downstream mortality risk. The objective was to determine the relationship between COVID-19 infection and 12-month mortality after recovery from the initial episode of COVID-19 in adult patients.
>
> Methods: An analysis of electronic health records (EHR) was performed for a cohort of 13,638 patients, including COVID-19 positive and a comparison group of COVID-19 negative patients, who were followed for 12 months post COVID-19 episode at one health system. Both COVID-19 positive patients and COVID-19 negative patients were PCR validated. COVID-19 positive patients were classified as severe if they were hospitalized within the first 30 days of the date of their initial positive test. The 12-month risk of mortality was assessed in unadjusted Cox regressions and those adjusted for age, sex, race and comorbidities. Separate subgroup analyses were conducted for (a) patients aged 65 and older and (b) those <65 years.

> Results: Of the 13,638 patients included in this cohort, 178 had severe COVID-19, 246 had mild/moderate COVID-19, and 13,214 were COVID-19 negative. In the cohort, 2,686 died in the 12-month period. The 12-month adjusted all-cause mortality risk was significantly higher for patients with severe COVID-19 compared to both COVID-19 negative patients (HR 2.50; 95% CI 2.02, 3.09) and mild COVID-19 patients (HR 1.87; 95% CI 1.28, 2.74). The vast majority of deaths (79.5%) were for causes other than respiratory or cardiovascular conditions. Among patients aged <65 years, the pattern was similar but the mortality risk for patients with severe COVID-19 was increased compared to both COVID-19 negative patients (HR 3.33; 95% CI 2.35, 4.73) and mild COVID-19 patients (HR 2.83; 95% CI 1.59, 5.04). Patients aged 65 and older with severe COVID-19 were also at increased 12-month mortality risk compared to COVID-19 negative patients (HR 2.17; 95% CI 1.66, 2.84) but not mild COVID-19 patients (HR 1.41; 95% CI 0.84, 2.34).
>
> Discussion: Patients with a COVID-19 hospitalization were at significantly increased risk for future mortality. In a time when nearly all COVID-19 hospitalizations are preventable this study points to an important and under-investigated sequela of COVID-19 and the corresponding need for prevention."

JACC Heart Fail: Use of Cardiopulmonary Stress Testing for Patients With Unexplained Dyspnea Post–Coronavirus Disease (29 November 2021)

> "Objectives: The authors used cardiopulmonary exercise testing (CPET) to define unexplained dyspnea in patients with post-acute sequelae of severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection (PASC). We assessed participants for criteria to diagnose myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS).
>
> Background: Approximately 20% of patients who recover from coronavirus disease (COVID) remain symptomatic. This syndrome is named PASC. Its etiology is unclear. Dyspnea is a frequent symptom.
>
> Methods: The authors performed CPET and symptom assessment for ME/CFS in 41 patients with PASC 8.9 ± 3.3 months after COVID. All patients had normal pulmonary function tests, chest X-ray, and chest computed tomography scans. Peak oxygen consumption (peak VO2), slope of minute ventilation to CO2 production (VE/VCO2 slope), and end tidal pressure of CO2 (PetCO2) were measured. Ventilatory patterns were reviewed with dysfunctional breathing defined as rapid erratic breathing.
>
> Results: Eighteen men and 23 women (average age: 45 ± 13 years) were studied. Left ventricular ejection fraction was 59% ± 9%. Peak VO2 averaged 20.3 ± 7 mL/kg/min (77% ± 21% predicted VO2). VE/VCO2 slope was 30 ± 7. PetCO2 at rest was 33.5 ± 4.5 mm Hg. Twenty-four patients (58.5%) had a peak VO2 <80% predicted. All patients with peak VO2 <80% had a circulatory limitation to exercise. Fifteen of 17 patients with normal peak VO2 had ventilatory abnormalities including peak respiratory rate >55 (n = 3) or dysfunctional

> breathing (n = 12). For the whole cohort, 88% of patients (n = 36) had ventilatory abnormalities with dysfunctional breathing (n = 26), increased VE/VCO2 (n = 17), and/or hypocapnia PetCO2 <35 (n = 25). Nineteen patients (46%) met criteria for ME/CFS.
>
> Conclusions: Circulatory impairment, abnormal ventilatory pattern, and ME/CFS are common in patients with PASC. The dysfunctional breathing, resting hypocapnia, and ME/CFS may contribute to symptoms. CPET is a valuable tool to assess these patients."

Clin Infect Dis: Phenotyping of acute and persistent COVID-19 features in the outpatient setting: exploratory analysis of an international cross-sectional online survey (26 November 2021)

> "Background: Long COVID, defined as presence of COVID-19 symptoms 28 days or more after clinical onset, is an emerging challenge to healthcare systems. The objective of this study was to explore recovery phenotypes in non-hospitalized COVID-19 individuals.
>
> Methods: A dual cohort, online survey study was conducted between September 2020 and July 2021 in the neighboring European regions Tyrol (TY, Austria, n = 1157) and South Tyrol (STY, Italy, n = 893). Data on demographics, comorbidities, COVID-19 symptoms and recovery adult outpatients were collected. Phenotypes of acute COVID-19, post-acute sequelae and risk of protracted recovery were explored by semi-supervised clustering and multi-parameter LASSO modeling.
>
> Results: Working age subjects (TY: 43 yrs (IQR: 31 - 53), STY: 45 yrs (IQR: 35 - 55)) and females (TY: 65.1%, STY: 68.3%) predominated the study cohorts. Nearly half of the participants (TY: 47.6%, STY: 49.3%) reported symptom persistence beyond 28 days. Two acute COVID-19 phenotypes were discerned: the non-specific infection phenotype and the multi-organ phenotype (MOP). Acute MOP symptoms encompassing multiple neurological, cardiopulmonary, gastrointestinal and dermatological complaints were linked to elevated risk of protracted recovery. The major subset of long COVID individuals (TY: 49.3%, STY: 55.6%) displayed no persistent hyposmia or hypogeusia but high counts of post-acute MOP symptoms and poor self-reported physical recovery.
>
> Conclusion: The results of our two-cohort analysis delineated phenotypic diversity of acute and post-acute COVID-19 manifestations in home-isolated patients which needs to be considered for predicting protracted convalescence and allocation of medical resources."

J Clin Med: Phantosmia, Parosmia, and Dysgeusia Are Prolonged and Late-Onset Symptoms of COVID-19 (12 November 2021)

> "Deficiencies in smell and taste are common symptoms of COVID-19. Quantitative losses are well surveyed. This study focuses on qualitative changes such as phantosmia (hallucination of smell), parosmia (alteration of smell), and dysgeusia (alteration of taste) and possible connections with the adaptive immune system. Subjective experience of deficiency in taste and smell was assessed by two different questionnaires after a median of 100 and 244 days

> after first positive RT-PCR test. SARS-CoV-2-specific antibody levels were measured with the iFlash-SARS-CoV-2 assay. After 100 days a psychophysical screening test for olfactory and gustatory dysfunction was administered. 30 of 44 (68.2%) participants reported a chemosensory dysfunction (14 quantitative, 6 qualitative, 10 quantitative, and qualitative) during COVID-19, eleven (25.0%) participants (1 quantitative, 7 qualitative, 3 quantitative, and quantity) after 100 days, and 14 (31.8%) participants (1 quantitative, 10 qualitative, 3 quantitative and qualitative) after 244 days. Four (9.1%) participants, who were symptom-free after 100 days reported now recently arisen qualitative changes. Serological and T-cell analysis showed no correlation with impairment of taste and smell. In conclusion, qualitative changes can persist for several months and occur as late-onset symptoms months after full recovery from COVID-19-induced quantitative losses in taste and smell."

Pediatric Population

News in Brief

"US pediatric COVID-19 cases continue to climb" (CIDRAP; see also: AAP data).

"What you can expect when vaccines become available for kids under 5" (NPR).

Pfizer released follow-up data on vaccine safety and efficacy in adolescents (Pfizer).

Journal Articles

Lancet Respir Med: Risk of COVID-19 hospital admission among children aged 5–17 years with asthma in Scotland: a national incident cohort study (30 November 2021)

> "Background: There is an urgent need to inform policy deliberations about whether children with asthma should be vaccinated against SARS-CoV-2 and, if so, which subset of children with asthma should be prioritised. We were asked by the UK's Joint Commission on Vaccination and Immunisation to undertake an urgent analysis to identify which children with asthma were at increased risk of serious COVID-19 outcomes.
>
> Methods: This national incident cohort study was done in all children in Scotland aged 5–17 years who were included in the linked dataset of Early Pandemic Evaluation and Enhanced Surveillance of COVID-19 (EAVE II). We used data from EAVE II to investigate the risk of COVID-19 hospitalisation among children with markers of uncontrolled asthma defined by either previous asthma hospital admission or oral corticosteroid prescription in the previous 2 years. A Cox proportional hazard model was used to derive hazard ratios (HRs) and 95% CIs for the association between asthma and COVID-19 hospital admission, stratified by

> markers of asthma control (previous asthma hospital admission and number of previous prescriptions for oral corticosteroids within 2 years of the study start date). Analyses were adjusted for age, sex, socioeconomic status, comorbidity, and previous hospital admission.
>
> Findings: Between March 1, 2020, and July 27, 2021, 752 867 children were included in the EAVE II dataset, 63 463 (8·4%) of whom had clinician-diagnosed-and-recorded asthma. Of these, 4339 (6·8%) had RT-PCR confirmed SARS-CoV-2 infection. In those with confirmed infection, 67 (1·5%) were admitted to hospital with COVID-19. Among the 689 404 children without asthma, 40 231 (5·8%) had confirmed SARS-CoV-2 infections, of whom 382 (0·9%) were admitted to hospital with COVID-19. The rate of COVID-19 hospital admission was higher in children with poorly controlled asthma than in those with well controlled asthma or without asthma. When using previous hospital admission for asthma as the marker of uncontrolled asthma, the adjusted HR was 6·40 (95% CI 3·27–12·53) for those with poorly controlled asthma and 1·36 (1·02–1·80) for those with well controlled asthma, compared with those with no asthma. When using oral corticosteroid prescriptions as the marker of uncontrolled asthma, the adjusted HR was 3·38 (1·84–6·21) for those with three or more prescribed courses of corticosteroids, 3·53 (1·87–6·67) for those with two prescribed courses of corticosteroids, 1·52 (0·90–2·57) for those with one prescribed course of corticosteroids, and 1·34 (0·98–1·82) for those with no prescribed course, compared with those with no asthma.
>
> Interpretation: School-aged children with asthma with previous recent hospital admission or two or more courses of oral corticosteroids are at markedly increased risk of COVID-19 hospital admission and should be considered a priority for vaccinations. This would translate into 9124 children across Scotland and an estimated 109 448 children across the UK."
>
> See also: commentary

Clin Infect Dis: Acute and persistent symptoms in children with PCR-confirmed SARS-CoV-2 infection compared to test-negative children in England: active, prospective, national surveillance (29 November 2021)

> "Background: Most children recover quickly after COVID-19, but some may have on-going symptoms. Follow-up studies have been limited by small sample sizes and lack of appropriate controls.
>
> Methods: We used national testing data to identify children aged 2-16 years with a SARS-CoV-2 PCR test during 01-07 January 2021 and randomly selected1,500 PCR-positive cases and 1,500 matched PCR-negative controls. Parents were asked to complete a questionnaire about the acute illness and pre-specified neurological, dermatological, sensory, respiratory, cardiovascular, gastrointestinal, mental health (including emotional and behavioural well-being) and other symptoms experienced at least five times at one month after the PCR test.

> Results: Overall, 35.0% (859/2456) completed the questionnaire, including 38.0% (472/1242) cases and 32% (387/1214) controls. of whom 68% (320/472) and 40% (154/387) were symptomatic, respectively. The most prevalent acute symptoms were cough (249 /859, 29.0%), fever (236/859, 27.5%), headache (236/859, 27.4%) and fatigue (231/859, 26.9%). One month later, 21/320 (6.7%) of symptomatic cases and 6/154 (4.2%) of symptomatic controls (p=0.24) experienced on-going symptoms. Of the 65 on-going symptoms solicited, three clusters were significantly (p<0.05) more common, albeit at low prevalence, among symptomatic cases (3-7%) than symptomatic controls (0-3: neurological, sensory and emotional and behavioural wellbeing. Mental health symptoms were reported by all groups but more frequently among symptomatic cases than symptomatic controls or asymptomatic children.
>
> Conclusions: Children with symptomatic COVID-19 had a slightly higher prevalence of on-going symptoms than symptomatic controls, and not as high as previously reported. Healthcare resources should be prioritised to support the mental health of children."

Clin Infect Dis: Epidemiology of Acute Myocarditis/Pericarditis in Hong Kong Adolescents Following Comirnaty Vaccination (28 November 2021)

> "Background: Age-specific incidence of acute myocarditis/pericarditis in adolescents following Comirnaty vaccination in Asia is lacking. This study aimed to study the clinical characteristics and incidence of acute myocarditis/pericarditis among Hong Kong adolescents following Comirnaty vaccination.
>
> Methods: This is a population cohort study in Hong Kong that monitored adverse events following immunization through a pharmacovigilance system for COVID-19 vaccines. All adolescents aged between 12 and 17 years following Comirnaty vaccination were monitored under the COVID-19 vaccine Adverse Event Response and Evaluation Programme. The clinical characteristics and overall incidence of acute myocarditis/pericarditis in adolescents following Comirnaty vaccination were analysed.
>
> Results: Between 14 June 2021 and 4 September 2021, 33 Chinese adolescents who developed acute myocarditis/pericarditis following Comirnaty vaccination were identified. 29 (87.88%) were males and 4 (12.12%) were females, with a median age of 15.25 years. 27 (81.82%) and 6 (18.18%) cases developed acute myocarditis/pericarditis after receiving the second and first dose, respectively. All cases are mild and required only conservative management.The overall incidence of acute myocarditis/pericarditis was 18.52 (95% Confidence Interval [CI], 11.67-29.01) per 100,000 persons vaccinated. The incidence after the first and second doses were 3.37 (95%CI 1.12-9.51) and 21.22 (95%CI 13.78-32.28 per 100,000 persons vaccinated, respectively. Among male adolescents, the incidence after the first and second doses were 5.57 (95% CI 2.38-12.53) and 37.32 (95% CI 26.98-51.25) per 100,000 persons vaccinated.

> Conclusions: There is a significant increase in the risk of acute myocarditis/pericarditis following Comirnaty vaccination among Chinese male adolescents, especially after the second dose."

JAMA Netw Open: Seroprevalence of SARS-CoV-2 Antibodies Among Children in School and Day Care in Montreal, Canada (23 November 2021)

> "Question: What is the seroprevalence of SARS-CoV-2 antibodies in a convenience sample of children aged 2 to 17 years in Montreal, Canada, enrolled between October 2020 and March 2021?
>
> Findings: In this cohort study of 1632 participants, the mean baseline seroprevalence of SARS-CoV-2 was 5.8%. Of the 95 participants who were seropositive for SARS-CoV-2 antibodies, 82% were not tested or tested negative, and all experienced either mild or no clinical symptoms.
>
> Meaning: The findings suggest that there was more transmission occurring in children compared with what was being detected, although children experienced few or mild symptoms."

Healthcare Workers

Journal Articles

Infect Control Hosp Epidemiol: Evolution of SARS-CoV-2 Seroprevalence Among Employees of a United States Academic Children's Hospital During the COVID-19 Pandemic (02 December 2021)

> "Objectives: Describe cumulative seroprevalence of SARS-CoV-2 antibodies during the COVID-19 pandemic among employees of a large pediatric healthcare system.
>
> Design, setting, and participants: Prospective observational cohort study open to adult employees at Children's Hospital of Philadelphia, conducted April 20 - December 17, 2020.
>
> Methods: Employees were recruited starting with high-risk exposure groups, utilizing emails, flyers, and announcements at virtual town halls. At baseline, 1-month, 2-month, and 6-month timepoints, participants reported occupational and community exposures and gave a blood sample for SARS-CoV-2 antibody measurement by enzyme-linked immunosorbent assays (ELISAs). A post hoc Cox proportional hazards regression model was performed to identify factors associated with increased risk for seropositivity.
>
> Results: 1740 employees were enrolled. At 6-months, cumulative seroprevalence was 5.3%, below estimated community point seroprevalence; seroprevalence was 5.8% and 3.4%

> among employees with and without direct patient care, respectively. Most participants seropositive at baseline remained positive at follow-up assessments. In post hoc analysis, direct patient care (HR: 1.95, 95% CI: 1.03 to 3.68), Black race (HR: 2.70, 95% CI: 1.24 to 5.87), and exposure to a confirmed case in a non-healthcare setting (HR: 4.32, 95% CI: 2.71 to 6.88) were associated with statistically significant increased risk for seropositivity.
>
> Conclusions: Employee SARS-CoV-2 seroprevalence rates remained below the surrounding community's point prevalence rates. Provision of direct patient care, Black race, and exposure to a confirmed case in non-healthcare setting conferred increased risk. These data can inform occupational protection measures to maximize protection of employees within the workplace during future COVID waves or other epidemics."

Infect Control Hosp Epidemiol: Is COVID-19 Vaccination Rate Among Healthcare Personnel Reflective of their Respective Community? An Evaluation of a Multistate Healthcare System (02 December 2021)

> "COVID-19 vaccination rates of a large health system reflected their respective service areas but varied by work role. Nurse vaccination rates were higher (56.9%) while nursing support personnel were lower (38.6%) than their communities (51.7%; P<0.001). Physician vaccination rates were highest (71.6%) and not associated with community vaccination levels."

JAMA Netw Open: Factors Associated With COVID-19 Vaccine Receipt by Health Care Personnel at a Major Academic Hospital During the First Months of Vaccine Availability (01 December 2021)

> "Question: What was the COVID-19 vaccine uptake among health care personnel (HCP) shortly after availability, and what factors were associated with uptake?
>
> Findings: In this cross-sectional study of 12 610 HCP at a major US academic hospital, two-thirds received a first dose within the first 4 months; 98% of those received 2 doses. Adjusted for age, sex, job position, and area-level social vulnerability, Black or African American and multiracial HCP were less likely to receive the vaccine compared with White HCP, with narrower disparities observed for nurses and no disparities found among physicians.
>
> Meaning: These findings indicate the presence of racial and ethnic disparities in HCP vaccine uptake, except among physicians."

JAMA Netw Open: Morally Injurious Experiences and Emotions of Health Care Professionals During the COVID-19 Pandemic Before Vaccine Availability (24 November 2021)

> "Question: How did health care workers experience moral injury during the COVID-19 pandemic before the availability of vaccines?

> Findings: In this qualitative study of 1344 health care professionals in 2020, respondents reported significant changes in their personal and professional lives during the course of the pandemic. Common themes were feeling isolated from non–health care professionals, alienated from patients, and betrayed by coworkers, administrators, and the public.
>
> Meaning: Moral injury can result from chronic stressors in morally injurious environments; leadership must identify and address these stressors to effectively support health care professionals as COVID-19 continues to strain staff's physical, mental, and emotional resources."

JAMA Netw Open: Mental Health Outcomes Among Italian Health Care Workers During the COVID-19 Pandemic (24 November 2021)

> "Question: What are the mental health outcomes among Italian health care workers during the COVID-19 pandemic?
>
> Findings: In this longitudinal cohort study of 2856 health care workers in Italy during the COVID-19 pandemic the prevalence of depression symptoms, anxiety symptoms, insomnia symptoms, and posttraumatic stress symptoms decreased among Italian health care workers 14 months after the beginning of the COVID-19 pandemic. Prolonged work with patients with COVID-19 was significantly associated with mental health outcomes, whereas quitting work as a frontline health care worker was significantly associated with decrease in mental health issues.
>
> Meaning: These findings help to identify the potential risk factors for health care workers exposed to direct contact with patients with COVID-19 and could help inform better preventive policies regarding mental health in this particular population."

JAMA Netw Open: Patient and Health Care Worker Perceptions of Communication and Ability to Identify Emotion When Wearing Standard and Transparent Masks (22 November 2021)

> "Question: Could transparent masks help to overcome communication barriers associated with widespread mask use among the general population, general health care workers, and health care workers who are deaf or hard of hearing in the United States?
>
> Findings: In this survey study of 1000 members of the general public, 123 general health care workers, and 45 health care workers who are deaf or hard of hearing, participants perceived mask wearing as potentially impairing communication. Respondents reported an improved ability to read emotion with transparent mask use, and transparent masks were generally accepted across all 3 populations surveyed.
>
> Meaning: These findings suggest that transparent masks have the potential to overcome barriers in communication brought on by universal mask wearing during the COVID-19 pandemic."

↑ Back to Table of Contents

Disparities and Health Equity

News in Brief

"Omicron brings COVID-19 vaccine inequity 'home to roost'" (AP).

The UK's health secretary has called for a racial bias review in Covid deaths: "Medical devices 'made for white people' may have driven higher minority fatality rates" (The Times).

The December issue of *AMA Journal of Ethics* focuses on 'health justice and diversity in medical school admissions' (AMA J Ethics).

Long read: "A tale of two pandemics: the true cost of Covid in the global south" (Guardian).

Journal Articles

JAMA Netw Open: Variation in COVID-19 Mortality in the US by Race and Ethnicity and Educational Attainment (22 November 2021)

> "Question: How did COVID-19 mortality rates during 2020 in the United States vary by race and ethnicity in combination with educational attainment?
>
> Findings: In this cross-sectional study of 219.1 million adults aged 25 years or older, most racial and ethnic minority populations had higher age-adjusted mortality rates than non-Hispanic White populations, including when comparing within levels of educational attainment. If all racial and ethnic populations had experienced the same mortality rates as college-educated non-Hispanic White populations, 71% fewer deaths among racial and ethnic minority populations would have occurred.
>
> Meaning: This study suggests that public health research and practice should attend to the ways in which populations that share socioeconomic characteristics may still experience racial and ethnic inequity in COVID-19 mortality rates."

Soc Sci Med: COVID-19 and the Nordic Paradox: a call to measure the inequality reducing benefits of welfare systems in the wake of the pandemic (November 2021; online 04 October 2021)

> "The Nordic Paradox of inequality describes how the Nordic countries have puzzlingly high levels of relative health inequalities compared to other nations, despite extensive universal welfare systems and progressive tax regimes that redistribute income. However, the veracity and origins of this paradox have been contested across decades of literature, as many scholars argue it relates to measurement issues or historical coincidences. Disentangling between potential explanations is crucial to determine if widespread adoption of the Nordic model could represent a sufficient panacea for lowering health

> inequalities, or if new approaches must be pioneered. As newfound challenges to welfare systems continue to emerge, evidence describing the benefits of welfare systems is becoming ever more important. Preliminary evidence indicates that the COVID-19 pandemic is drastically exacerbating social inequalities in health across the world, via direct and indirect effects. We argue that the COVID-19 pandemic therefore represents a unique opportunity to measure the value of welfare systems in insulating their populations from rising social inequalities in health. However, COVID-19 has also created new measurement challenges and interrupted data collection mechanisms. Robust academic studies will therefore be needed-drawing on novel data collection methods-to measure increasing social inequalities in health in a timely fashion. In order to assure that policies implemented to reduce inequalities can be guided by accurate and updated information, policymakers, academics, and the international community must work together to ensure streamlined data collection, reporting, analysis, and evidence-based decision-making. In this way, the pandemic may offer the opportunity to finally clarify some of the mechanisms underpinning the Nordic Paradox, and potentially more firmly establish the merits of the Nordic model as a global example for reducing social inequalities in health."

Risk, Transmission, and Exposure

News in Brief

"Seven doctors contract Covid after attending Florida anti-vaccine summit" (Guardian).

Journal Articles

Infect Control Hosp Epidemiol: Continuously Active Disinfectant Inactivates SARS-CoV-2 and Human Coronavirus 229E Two Days After the Disinfectant Was Applied and Following Wear Exposures (02 December 2021)

> "The surface environment in COVID-19 patient's rooms may be persistently contaminated despite disinfection. A continuously active disinfectant demonstrated excellent sustained antiviral activity following a 48-hour period of wear and abrasion exposures with reinoculations. Reductions of >4-log10 were achieved within a 1-minute contact time for SARS-CoV-2 and the human coronavirus, 229E."

BMJ: Elapsed time since BNT162b2 vaccine and risk of SARS-CoV-2 infection: test negative design study (25 November 2021)

> "Objectives: To determine whether time elapsed since the second injection of the Pfizer-BioNTech BNT162b2 mRNA vaccine was significantly associated with the risk of covid-19 infection after vaccination in people who received two vaccine injections.
>
> Participants: Adults aged ≥18 years who had received a reverse transcription polymerase chain reaction (RT-PCR) test between 15 May 2021 and 17 September 2021, at least three weeks after their second vaccine injection, had not received a third vaccine injection, and had no history of covid-19 infection.
>
> Main outcome measures: Positive result for the RT-PCR test. Individuals who tested positive for SARS-CoV-2 and controls were matched for week of testing, age category, and demographic group (ultra-orthodox Jews, individuals of Arab ancestry, and the general population). Conditional logistic regression was adjusted for age, sex, socioeconomic status, and comorbid conditions.
>
> Results: 83 057 adults received an RT-PCR test for SARS-CoV-2 during the study period and 9.6% had a positive result. Time elapsed since the vaccine injection was significantly longer in individuals who tested positive (P<0.001). Adjusted odds ratio for infection at time intervals >90 days since vaccination were significantly increased compared with the reference of <90 days: 2.37 (95% confidence interval 1.67 to 3.36) for 90-119 days, 2.66 (1.94 to 3.66) for 120-149 days, 2.82 (2.07 to 3.84) for 150-179 days, and 2.82 (2.07 to 3.85) for ≥180 days (P<0.001 for each 30 day interval).
>
> Conclusions: In this large population of adults tested for SARS-CoV-2 by RT-PCR after two doses of mRNA BNT162b2 vaccine, a gradual increase in the risk of infection was seen for individuals who received their second vaccine dose after at least 90 days."

Clin Infect Dis: Infectious SARS-CoV-2 Virus in Symptomatic COVID-19 Outpatients: Host, Disease, and Viral Correlates (23 November 2021)

> "Background: While SARS-CoV-2 infectious virus isolation in outpatients with COVID-19 has been associated with viral RNA levels and symptom duration, little is known about the host, disease and viral determinants of infectious virus detection.
>
> Methods: COVID-19 adult outpatients were enrolled within 7 days of symptom onset. Clinical symptoms were recorded via patient diary. Nasopharyngeal swabs were collected to quantitate SARS-CoV-2 RNA by reverse transcriptase polymerase chain reaction and for infectious virus isolation in Vero E6-cells. SARS-CoV-2 antibodies were measured in serum using a validated ELISA assay.
>
> Results: Among 204 participants with mild-to-moderate symptomatic COVID19, the median nasopharyngeal viral RNA was 6.5 (IQR 4.7-7.6 log10 copies/mL), and 26% had detectable SARS-CoV-2 antibodies (IgA, IgM, IgG, and/or total Ig) at baseline. Infectious virus was recovered in 7% of participants with SARS-CoV-2 antibodies compared to 58% of

> participants without antibodies (prevalence ratio (PR)=0.12, 95% CI: 0.04, 0.36; p=0.00016). Infectious virus isolation was also associated with higher levels of viral RNA (mean RNA difference +2.6 log10, 95% CI: 2.2, 3.0; p<0.0001) and fewer days since symptom onset (PR=0.79, 95% CI: 0.71, 0.88 per day; p<0.0001).
>
> Conclusions: The presence of SARS-CoV-2 antibodies is strongly associated with clearance of infectious virus. Seropositivity and viral RNA levels are likely more reliable markers of infectious virus clearance than subjective measure of COVID-19 symptom duration. Virus-targeted treatment and prevention strategies should be administered as early as possible and ideally before seroconversion."

Other Infectious Diseases and Public Health Issues

News in Brief

Comment: "Africa: tackle HIV and COVID-19 together — Failure to get COVID-19 vaccines to nations with high rates of uncontrolled advanced HIV puts people living with that virus at even greater risk, and could drive the emergence of coronavirus variant" (Nature).

A yellow fever outbreak in Ghana has a 202 suspected cases, 70 confirmed and 35 fatal (WHO).

"FDA proposes changes to Food Safety Modernization Act Rule to enhance safety of agricultural water used on produce" (FDA).

"Public health worker recruitment major focus of Senate's new BIO Preparedness Workforce Act" (HPN).

Journal Articles

MMWR: Vital Signs: HIV Infection, Diagnosis, Treatment, and Prevention Among Gay, Bisexual, and Other Men Who Have Sex with Men — United States, 2010–2019 (03 December 2021)

> "What is already known about this topic? Gay, bisexual, and other men who have sex with men (MSM) are disproportionately affected by HIV.
>
> What is added by this report? This analysis of national surveillance data found that the estimated number of new HIV infections among MSM did not change overall during 2010–2019; infections decreased among White MSM but not among Black MSM or Hispanic/Latino MSM. Most measures of use of HIV prevention and treatment services were lower among Black MSM and Hispanic/Latino MSM than White MSM and younger MSM compared with other age groups.

> What are the implications for public health practice? Improving access to and use of HIV services for MSM, particularly Black MSM, Hispanic/Latino MSM, and younger MSM, is essential to ending the HIV epidemic in the United States."

MMWR: Enterovirus D68-Associated Acute Respiratory Illness – New Vaccine Surveillance Network, United States, July–November 2018–2020 (26 November 2021)

> "What is already known about this topic? Enterovirus D68 (EV-D68) is associated with acute respiratory illness (ARI) and acute flaccid myelitis. Annual U.S. detections of EV-D68 in respiratory specimens vary; biennial circulation was observed during 2014–2018.
>
> What is added by this report? During July–November 2019 and 2020, six and 30 EV-D68 detections, respectively, were identified in children with ARI enrolled in the seven New Vaccine Surveillance Network sites, representing 0.2% and 1.4% of children with ARI; most patients with EV-D68 were Hispanic or Black persons.
>
> What are the implications for public health practice? EV-D68 is an important pediatric pathogen causing respiratory disease. Circulation in 2020 was lower than anticipated; implications for future circulation are unknown. Continued monitoring and characterization of EV-D68 are critical."

Statistics

	Total Cases	*Total Deaths*	*Total Vaccine Doses Administered*
Global	264,395,908	5,238,447	8,107,919,857
United States	48,833,058	785,914	462,174,438

JHU CSSE as of 1000 EDT 03 December 2021

Virginia	Total cases (state)	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	976,599	29,938	15,582	21,289	25,250	13,068	11,299	51,756
Hospitalizations	39,887	1,336	710	797	1,382	934	720	2,669
Deaths	14,753	371	249	306	359	250	249	574

VA DOH as of 1000 EDT 03 December 2021

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